Kitta T¹, Tanaka H¹, Mitsui T¹, Kannno Y¹, Moriya K¹, Nonomura K¹, Yoshimura N²

1. Department of Renal and Genitourinary Surgery, Graduate School of Medicine, Hokkaido University, **2.** Department of Urology, University of Pittsburgh School of Medicine

TIME-COURSE EVALUATION OF URETHRAL FUNCTIONAL RECOVERY FROM THE EFFECT OF SIMULATED BIRTH TRAUMA AND OVARIECTOMY ON SNEEZE-INDUCED STRESS URINARY INCONTINENCE (SUI) IN RATS

Hypothesis / aims of study

Pregnancy and vaginal childbirth are frequently seen as causes of stress urinary incontinence (SUI); however the exact mechanism by which urethral function is damaged remains unknown. We therefore performed a detailed time-course evaluation of urethral functional recovery from the effect of simulated birth trauma with or without ovariectomy (OVX) using a rat model of sneeze-induced SUI.

Study design, materials and methods

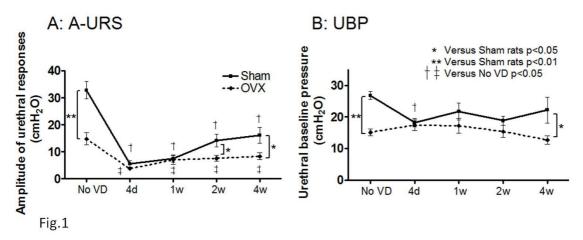
Female Sprague-Dawley rats underwent bilateral OVX or sham operation. Four days, 1, 2 and 4 weeks after vaginal distension (VD) induced by balloon catheter inflation in the vagina, urethral responses and sneeze-induced leak point pressure (S-LPP) were evaluated. Sneeze reflex was induced by a rat's whisker cut and inserted into the nostril. Urethral responses were measured using a microtransducer-tipped catheter inserted to the middle urethra from the urethral orifice. The amplitude of urethral responses during sneezing (A-URS) and urethral baseline pressure (UBP) was evaluated.

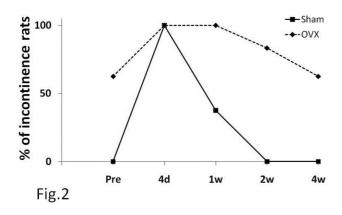
Results

Four days after VD, A-URS and UBP were significant decreased compared with control (no-VD) values (Fig. 1), and all rats showed SUI during sneezing in both sham and OVX groups (Fig. 2). However, no leakage was observed 2 or 4 weeks after VD in sham rats, in which UBP was recovered after 1 week, but A-URS was still significantly decreased up to 4 weeks after VD. In contrast, 5 of 8 OVX rats had SUI during sneezing 4 weeks after VD in association with a significant reduction of A-URS. When compared with sham rats, A-URS were significantly lower at 2 and 4 weeks after VD, associated with significantly lower UBP at 4 weeks after VD in OVX rats.

Interpretation of results

Clinically, although SUI after vaginal childbirth is common, it is usually short-lasting in most women and reappears during post-menoposal years in women who have given birth to their children in an earlier age. In this study, sneeze-induced urethral striated muscle reflexes (represented by A-URS) are still impaired even after VD-induced SUI disappeared in sham rats, suggesting that the damage of urethral continence mechanisms remain even after the recovery from SUI after vaginal birth trauma. In addition, estrogen deficiency induced by OVX further impairs both striated muscle urethral reflex activity (represented by A-URS) and smooth muscle urethral activity (represented by UBP), resulting in the delay of the recovery from VD-induced damage of urethral continence reflex, and continued SUI after VD in OVX rats. Thus it seems likely that estrogen deficiency contributes to overt SUI as an additional factor for impairment of urethral continence mechanisms, which are insidiously damaged after simulated birth trauma.





<u>Concluding message</u>
The results of the present study suggest that the functional impairment of striated muscle-mediated urethral continence reflexes persists despite the disappearance of SUI after vaginal birth trauma and that estrogen deficiency contribute as an additional factor to the full development of SUI conditions by further damaging striated and smooth muscle urethral continence mechanisms. These findings provide further insights into the pathophysiological process of SUI.

Specify source of funding or grant	NIH DK067226, AR049398 and DK055387
Is this a clinical trial?	No
What were the subjects in the study?	ANIMAL
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	Yes
Name of ethics committee	University of Pittsburgh Institutional Animal Care and Use Committee